REMARKS

Claims 1-4, 6-9, 11-12, and 14-15 are pending in the application. Claims 12 and 14-15 are withdrawn from consideration. Claims 1-4, 6-9 and 11 are rejected. Support for the amendment can be found in the Abstract, Field of the Invention, page 21, lines 27-29 of the specification, and Example 4B.

Claim Rejection – 35 U.S.C. 103(a)

Claims 1-9 and 11 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Kuo et al. in view of Masure et al.

Kuo et al. teach a composition comprising *Streptococcus pneumoniae* polysaccharides conjugated to pneumolysin and optionally an adjuvant. As the Examiner has noted, Kuo et al. do not teach the addition of further proteins, and thus the reference does not teach the addition of choline binding proteins. In fact Kuo et al. teach that:

> "conjugate vaccines of this invention are highly immunogenic in warm-blooded animals" and "The vaccines elicit antibodies to both the polysaccharide and the protein, recombinant pneumolysin". (see column 2, lines 32-35 of US 5,565,204).

Applicants respectfully submit that Kuo et al. teach to the skilled artisan that their *S. pneumoniae* polysaccharide-pneumolysin conjugate possesses all the desired characteristics that one would require for a vaccine – (i) immunogenicity to the polysaccharide and (ii) to the conjugated carrier protein. Conversely, Kuo et al. provides no motivation to add yet another component to a *Streptococcus pneumonia* polysaccharide-conjugate composition.

Furthermore, Applicants respectfully submit that in the vaccine arts, the skilled artisan is acutely aware that when administering an immunogenic composition to elicit a protective immune response (i.e., a vaccine), the fewer components that are combined to confer protection against infection, the better. From a regulatory point of view, regulatory agencies prefer fewer components, as that lessens the risk of unwanted side effects. From a scientific point of view, fewer components are better, because it is well known in the art that the risk of immunological interference (i.e. an decrease in immunological response to one or more components in a combination vaccine, relative to that component administered by itself) increases when more components are added to a vaccine. From a vaccine manufacturers

point of view, there is a clear benefit to using the minimum number of components to confer adequate protection. Thus, when Kuo et al. make statements that their invention is "highly immunogenic", what would be the motivation to add further components such as the choline binding proteins of Masure et al?

Masure et al disclose the use of choline binding proteins as a *Streptococcus pneumoniae* protein-based vaccine. That is, as alternative to polysaccharide (or polysaccharide conjugate) based vaccines. In fact, Masure et al. teach that a protein-based vaccine is superior to a (capsule or capsular) polysaccharide vaccine. See, e.g., column 2, lines 4-8 of Masure.

> "An alternative to whole bacterial vaccines are acellar vaccines or subunit vaccines in which the antigen includes a bacterial surface protein. These vaccines could potentially overcome the deficiencies of whole bacterial **or capsule-based vaccines**."

It is noted that Masure et al. also suggest a nucleic acid vaccine, and therapeutic use of choline binding antibodies, but Masure et al. *do not suggest* (i) a polysaccharide-based vaccine or (ii) the combination of a polysaccharide-based vaccine *and* a protein-based vaccine (see, e.g., column 24, lines 57-59, column 27, lines 55-61, Abstract of US 6,245,335).

Thus Applicants respectfully submit that there would be no motivation to combine the *S. pneumoniae* polysaccharide-protein conjugate of Kuo et al. with the *S. pneumoniae* protein antigen of Masure et al. to arrive at the claimed invention. Both references teach a *S. pneumoniae* vaccine composition – one based on polysaccharides (conjugated) and one based on free or unconjugated *S. pneumoniae* proteins. Both compositions appear to elicit good immune responses in their respective models. However, given the desire in the art to add the fewest possible antigenic components to a vaccine (as discussed above) there would be no motivation to add the polysaccharide conjugates of Kuo et al. to the choline binding proteins of Masure et al.

Thus, Applicants respectfully submit that the claimed invention is not obvious over Kuo et al. in view of Masure et al. for neither reference, alone or in combination, teach the claimed invention, as amended, which clearly requires: a) at least one *Streptococcus pneumoniae* polysaccharide-protein conjugate; b) at least one unconjugated *Streptococcus*

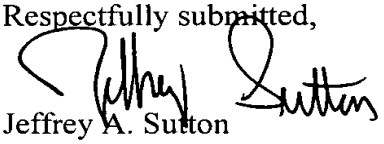
pneumoniae protein antigen; and c) an adjuvant which is a preferential inducer of a TH1 response.

It is further noted that the claimed invention discloses a surprisingly better immune response than the individual components, see e.g., Figure 1C, page 50, lines 10-16, page 53, lines 1-3 and page 55, lines 15-18 of the specification. This could not have been predicted based on the disclosures of Kuo et al. and Masure et al.

Thus, for all the reasons presented above, Applicants respectfully request that this rejection be withdrawn.

Applicants respectfully submit that the aforementioned amendments and remarks are fully responsive to the Office Action and request reconsideration of the rejections stated therein. The Examiner is invited to contact Applicants' undersigned at the telephone number provided below if such might facilitate allowance of the pending claims.

Respectfully submitted,



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